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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
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Additional inventors are being named on the 1 separately numbered sheets *attached hereto*

TITLE OF THE INVENTION (500 characters max)

TREATMENT FOR EAR DISORDERS

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ENCLOSED APPLICATION PARTS (check all that apply)

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☐ Application Date Sheet. See 37 CFR 1.76

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☒ No.

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[Page 1 of 2]

Respectfully *submitted*,

SIGNATURE

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Date JULY 14, 2004

REGISTRATION NO. 45,148 (*if* appropriate)

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TREATMENT OF EAR DISORDERS

FIELD OF THE INVENTION

The present invention relates to compositions and methods for the treatment of ear disorders, wherein the pharmacologically agent is administered to a treated ear in a form selected from a foam or mousse. These methods of administering a medicament in such forms increase the residence time of the medicament in the ear canal, enhance treatment effectiveness, increase compliance and are more convenient to use than currently available ear medications.

BACKGROUND OF THE INVENTION

Ear Structure

The ear, which is the organ of hearing and balance, consists of the outer, middle, and inner ear. The outer, middle, and inner ear function together to convert sound waves into nerve impulses that travel to the brain, where they are perceived as sound. The inner ear also helps to maintain balance. [The Merck Manual, Chapter 217.Biology of the Ears, Nose, and Throat.]

Outer Ear

The outer ear consists of the external part of the ear (pinna or auricle) and the ear canal (external auditory meatus). The pinna consists of cartilage covered by skin and is shaped to capture sound waves and funnel them through the ear canal to the eardrum (tympanic membrane), a thin membrane that separates the outer ear from the middle ear.

Middle Ear

The middle ear consists of the eardrum and a small air-filled chamber containing a chain of three tiny bones (ossicles) that connect the eardrum to the inner ear. The ossicles are named for their shapes. The hammer (malleus) is attached to the eardrum. The anvil (incus) is the middle bone between the hammer and the stirrup (stapes), which is attached to the oval window, a thin membrane at the entrance to the inner

ear. Vibrations of the eardrum are amplified mechanically by the ossicles and transmitted to the oval window. The middle ear further contains two tiny muscles. The tensor tympani muscle is attached to the hammer; it helps to tune and protect the ear. The stapedius muscle is attached to the stirrup and oval window; it contracts in response to a loud noise, making the chain of ossicles more rigid so that less sound is transmitted. This response, called the acoustic reflex, helps protect the delicate inner ear from sound damage.

The Eustachian tube, a small tube that connects the middle ear with the back of the nose, allows outside air to enter the middle ear. This tube, which opens when a person swallows, helps maintain equal air pressure on both sides of the eardrum and prevents fluid from accumulating in the middle ear. If air pressure is not equal, the eardrum may bulge or retract, which can be uncomfortable and distort hearing. Swallowing or voluntary "popping" of the ears can relieve pressure on the eardrum caused by sudden changes in air pressure, as often occurs when flying in an airplane. The eustachian tube's connection with the middle ear explains why upper respiratory infections (such as the common cold), which inflame and block the eustachian tube, can lead to middle ear infections or changes in middle ear pressure, resulting in pain.

Inner Ear

The inner ear (labyrinth) is a complex structure consisting of two major parts: the cochlea, the organ of hearing; and the vestibular system, the organ of balance. The vestibular system consists of the saccule and the utricle, which determine position sense, and the semicircular canals, which help maintain balance.

The cochlea, a hollow tube coiled in the shape of a snail's shell, is filled with fluid. Within the cochlea is the organ of Corti, which consists, in part, of about 20,000 specialized cells, called hair cells. These cells have small hairlike projections (cilia) that extend into the fluid. Sound vibrations transmitted from the ossicles in the middle ear to the oval window in the inner ear cause the fluid and cilia to vibrate. Hair cells in different parts of the cochlea vibrate in response to different sound frequencies and convert the vibrations into nerve impulses. The nerve impulses are transmitted along fibers of the cochlear nerve to the brain. Despite the protective effect of the acoustic reflex, loud noise can damage and destroy hair cells. Once a hair cell is destroyed, it

does not appear to regrow. Continued exposure to loud noise causes progressive damage, eventually resulting in hearing loss and sometimes noise or ringing in the ears (tinnitus).

The semicircular canals are three fluid-filled tubes at right angles to one another. Movement of the head causes the fluid in the canals to move. Depending on the direction the head moves, the fluid movement will be greater in one of the canals than in the others. The canals contain hair cells that respond to this movement of fluid. The hair cells initiate nerve impulses that tell the brain which way the head is moving, so that appropriate action can be taken to maintain balance. If the semicircular canals malfunction, as may occur in an upper respiratory infection and other conditions both temporary and permanent, a person's sense of balance may be lost or a whirling sensation (vertigo) may develop.

Use of Ear drops for the treatment of Ear Disorders

Currently, ear care products (ototopical agents) are administered to the treated subject in the form of drops. Generally, ear drops are based on antibiotic agents, antibacterial agents, antifungal agents, antiviral agents, steroid derivatives, anti-inflammatory agents, analgesic compounds or a mixture thereof. For example, initial therapy for AOE is typically an aminoglycoside combination consisting of neomycin, polymixin B and steroid (hydrocortisone, dexamethasone, Cortisporin, Dex-Otic, etc.) (Lee I, Steinberg I, Gill MA. Management of Ear Infections. Cal Parma 2001;spring; 56-64). Current medications also includes quinolones derivatives i.e. Ciprofloxacin 1% or Oflaxacine 0.3%. Other compositions of ear drops are further described in U.S. Pat. No. 6,521,213, the entire disclosure of which is hereby incorporated by reference.

Another common use of ear drops is for ear pain treatment. Ear pain (otalgia) can range from mild discomfort or a feeling of fullness to severe intense pain, and can be very unpleasant and even unbearable, especially in children. Usually, ear pain results from pathological conditions of the external or middle ear. Such pathological conditions, discussed lengthily above, may be caused by infection, trauma, or blockage of the ear. Briefly, common trauma may result by use of a cotton swab to clean the ear or as a result of sudden changes in pressure such as changes in altitude when flying or diving. Blockage of the ear canal can be caused by excessive earwax

or foreign objects such as beads, beans or bugs. Infections of the ears include otitis externa (swimmer's ear), otitis media, an infection of the inner ear, mastoiditis and other pathologies as mentioned above and fully described in the literature. Other disorders that may cause ear pain are allergic reactions, ruptured eardrum, acute sinusitis, chronic sinusitis, tooth abscess, sore throat with referred pain to the ears, Meniere's disease, tumors of the ear, which may be cancerous or benign and temporomandibular joint syndrome.

Currently available analgesic ear drops used for the treatment of ear pain usually contain analgesic compound such as: benzocaine 3-20%, tetracaine 0.5%, amethocaine 0.5% and analgesic like antipyrine 5% phenazone 0.5%. (for further details see: Medic. Bergman SH, editor. Shirol Publications Ltd, Herzliya Israel, Jan-Feb 2002).

The ear drops are usually administered to the treated ear by tilting the head of a treated subject to the side, instilling drops of the medicament into the ear and maintaining the adopted position for few minutes, in order to allow the medicine to reach the interior of the ear. A clean cotton-wool plug may be inserted into the opening of the ear to prevent the medication from leaking out. In addition, in order to prevent contamination of the ear drops, the bottle tip must not be in contact with any surface, including the hands and the ear itself.

A number of drawbacks are associated with ototopical administration in the form of drops. In principle, ear drops exert their effect by direct contact with affected area. If administration is poor (e.g., the head of the treated subject is not tilted long enough) and the drops cannot reach the infected area, the active agent cannot be effective. Delivery can be impaired in a number of different ways, including failure of the drops to enter the ear canal, short contact period of the medicament with the ear canal since the drops are naturally washed out or because the head of the treated subject is not tilted long enough for the agent to reach its target. In addition, the form of the current medicaments as ear drops is difficult to apply, especially to animals and little children who do not tend to cooperate mainly due to their disability to maintain a position for prolonged period (several minutes);and the cotton wool that is usually added to the ear after administering the drops, might be pushed inside the ear canal and could cause difficulties to removed. Also, the existing drugs often inadequately address a patient's

needs for efficacy and aesthetics (e.g. running of drops on face and neck), and the failure to address those needs may decrease patient compliance and impair overall treatment.

Thus, there is a widely recognized need for, and it would be highly advantageous to have a new convenient and practical form of medicaments to treat ear disorders, i.e. medicaments in a form of foam or mousse, that may counteract all drawbacks related to the use of such medicaments in the form of drops.

SUMMARY OF THE INVENTION

The present invention relates to novel delivery systems for providing a medicament for the treatment of ear disorders in general, and otitis externa, acute otitis media, serous otitis media, chronic suppurative otitis media, perichondritis, ear eczema, infections of the inner ear, mastoiditis, perforation of the eardrum (tympanic membrane), cholesteatoma, otosclerosis, otalgia caused by any physical or biological cause including without limiting: blockages, barotraumas, allergic reactions, acute sinusitis, chronic sinusitis, tooth abscess, sore throat with referred pain to the ears, Meniere's disease, myringitis, tumors, temporomandibular joint syndrome, temporal bone fracture and any other condition that requires administration of any kind of medicament into the ear canal of a treated subject in particular. According to the principles of the present invention the formulation and administration of such a medicament into the ear is in the form of a foam or mousse.

The application of a medicament in such forms allows prolonged contact of the active agent/s with the surface of the ear canal, and therefore enables non-frequent applications (e.g. once or twice a day only). The prolonged contact of the active agent/s with the affected area further facilitates rapid healing compared to the conventional treatment with ear drops. Furthermore, administration of such forms into the ear is much more convenient than the administration of drops, and makes it completely unnecessary either to tilt the head of a treated subject to the side during administration of the medicament, nor to plug the ear meatus with a cotton-wool or other plug, in order to prevent the medication from leaking out.

In certain embodiments of the current invention the medicament comprises at least one of the following: antibacterial agent, antibiotic agent, anti-fungal agent, steroid derivate agent, anti-inflammatory agent and analgetic agent or a mixture thereof of at least two of such agents, in the form of foam or mousse.

It is explicitly understood that the pharmaceutical composition and methods of the present invention are suitable for pharmacologically active agents whether water soluble, poorly water soluble or water insoluble. The judicious choice of ingredients will allow the use of a foam delivery whether or not active ingredients are water soluble or not. Combinations of active ingredients that are individually and independently water soluble or insoluble may also be practiced according to the present invention. There are many available solutions to the problem of formulation of poorly soluble ingredients for improved drug bioavailability including the use of surfactants, micelle solutions, emulsions, microemulsions and organic cosolvents, as are well known in the art of pharmaceutical formulations.

The medicament provided by the present invention, may be administered to the ear of the treated subject through a device in which the compositions are packed under pressure, suitable for application to the treated are in a form selected from a foam or mousse. Thus, according to another aspect the present invention provides a device or apparatus for administration of a medicament to the ear of a subject in the form of a foam comprising a container comprising the pharmaceutical composition and an extension, typically a tube extending therefrom, said extension adapted to access the ear in a convenient and gentle manner.

In one preferred embodiment of the invention, the medicament is administered to the treated subject in a metered dose manner.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, ear care medicaments in a foam-based formulation are provided. More specifically, the present invention provides a method for the treatment of ear disorder in a subject in need of such treatment comprising

administering an amount of a pharmaceutical composition in a form of foam through the external auditory meatus of said subject so as to thereby treat the subject.

As used herein, the term "foam" or "mousse" is defined as comprising any lightweight material in cellular form which is made by introducing gas bubbles into liquid.

The foam base formulations as opposed to ear drops offer an improved compliancy, i.e. the foam form could be applied infrequently to the treated area (e.g. once/twice daily) instead of frequent applications of current available ear drops (2-6 times a day). The foam-based formulation provides an improved administration to the treated subject, especially to little children and animals, since foam does not require special position, such as head tilting for several minutes. Furthermore, formulation in the form of a foam enable improved delivery of the medicament, so as the foam evaporates spontaneously after pre-determined period of time (by formulation), out of the ear without dripping. In addition, when the foam is applied to the ear, it does not leave any residue, stains or odor after it dries. Moreover, the uniqueness of the foam formulation is that there is a relatively uniform concentration of active ingredients at every site of the foam surface, hence the contact area of the active ingredient within the ear canal is effectively increased. The foam formulation further enables the active therapeutic agent/s to contact rapidly the treated area with substantially 100% coverage, and can improve penetration into the affected area.

Among other advantages, use of a foam-based formulation avoids the need and dangers of a cotton plug or wick, thus it dispenses with the use of such cotton which is uncomfortable and may lead to deep insertion of the cotton, and the need for a trained physician to pull it out.

In one embodiment of the invention, the treated ear disorder is any condition that requires administration of any pharmaceutical composition into the ear canal of the treated subject, so as to thereby treat the ear disorder. Such conditions include without limiting otitis externa, including acute otitis externa, acute otitis media, chronic suppurative otitis media, infections of the inner ear, mastoiditis, perforation of the tympanic membrane, ruptured eardrum, otalgia caused by any physical or biological cause as detailed previously including without limiting: allergic reactions, acute

sinusitis, chronic sinusitis, tooth abscess, sore throat with referred pain to the ears, Meniere's disease, tumors and temporomandibular joint syndrome.

In another embodiment, the pharmaceutical composition of the present invention is used to manufacture a medicament for the treatment of ear disorders which administered to the subject in need of such treatment in the form of foam.

In a further embodiment, the pharmaceutical composition of the present invention comprises one or more therapeutically active agent.

As used herein, the term "pharmaceutical composition" or "medicament" or "therapeutically active agent" or "active agent" or "agent", are all broadly used to mean any chemical or material that is desired to be applied, administered or used to treat ear disorder and can include, by way of illustration and not limitation any substance which is capable of altering a biologic, physiologic and/or immunologic function, and also substances generally referred to as pharmacologic agents and drugs, including antibiotic agents, antibacterial agents, antifungal agents, steroid agents, anti-inflammatory agents and local anesthetic agents.

In one embodiment of the invention, the therapeutically active agent is antibiotic agent. The antibiotic agent may be, for example, amikacin, gentamycin, tobramycin, streptomycin, netilmycin, kanamycin ciprofloxacin, norfloxacin, ofloxacin, trovafloxacin, lomefloxacin, levofloxacin, enoxacin, sulfonamides, polymyxin, chloramphenicol, neomycin, paramomomycin, colistimethate, bacitracin, vancomycin, tetracyclines, rifampins, cycloserine, beta-lactams, cephalosporins, and pharmaceutically acceptable derivatives thereof.

In a different embodiment, the active agent used in the provided method is antibacterial agent. Such antibacterial agent may be, for example, acetic acid or boric acid or a mixture thereof.

In yet, a different embodiment of the present invention, the active agent is a steroid. Such steroid includes without limiting betamethasone, betamethasone dipropionate, fluocinonide, fluocinoline acetonide, hydrocortisone, methylprednisolone, clobetasol, beclomethasone, dexamethasone sodium phosphate, triamcinolone and pharmaceutically acceptable derivatives thereof.

In one another embodiment, the therapeutically active agent is antifungal agent. The antifungal agent may be selected from the group consisting of amphotericins, fluconazole, flucytosine, natamycin, miconazole, ketoconazole, amphotericin B, nystatin, cromolyn, lodoxamide, levocabastin, naphazolin, antazoline, pheniramine and pharmaceutically acceptable derivatives thereof.

In a further embodiment, the therapeutically active agent is anti-inflammatory agent. Such agent may be, for example, any non steroidal anti-inflammatory agent (NSAID), antipyrin and pharmaceutically acceptable derivatives thereof. Examples of the non-steroidal antiinflammatory drug (NSAID) which is advantageously administered by the formulations of this invention include salicylic acid derivatives, such as, for example, aspirin; heteroaryl acetic acids, such as, for example, tolmetin, diclofenac, ketorolac; arylpropionic acids, such as, for example, ibuprofen, naproxen, flurbiprofen, ketoprofen, fenoprofen, oxaprozin; anthranilic acids (fenamates), such as, for example, mefenamic acid, meclofenamic acid, flufenamic acid; enolic acids, such as, for example, oxicams (e.g., piroxicam, tenoxicam), pyrazolidinediones (e.g., phenylbutazone, oxyphenthatrazone); alkanones, such as, for example, nabumetone. Among these, especially preferred, based on the current level of knowledge in the pharmacological arts, are ibuprofen, diclofenac, ketorolac, naproxen, flurbiprofen, ketoprofen and piroxicam. More generally, however, any of the government approved NSAIDs, such as listed in, for example, the most current edition of The Merck Index, may be advantageously used. In still, another embodiment of the invention, the active agent is a local anesthetic agent. Such agent may be selected, for example, from the group consisting of benzocaine, benzyl benzoate, bupivacaine, calamine, chloroprocaine, chloroxylenol, cinchocaine, cocaine, dexivacaine, diamocaine, dibucaine, dyclonine, etidocaine, hexylcaine, ketamine, levobupivacaine, lidocaine, menthol, mepivacaine, oxethazaine, phenol, pramoxine, prilocaine, amethocaine, tetracaine, proparacaine, propoxycaine, pyrrocaine, resorcinol, risocaine, rodocaine, ropivacaine, tetracaine, troclosan, and pharmaceutically acceptable derivatives thereof.

Compositions according to the present invention may also comprise any conventional carriers, excipients or adjuvant used in pharmaceuticals, personal care formulations

and compositions or veterinary formulations. These carriers, excipients and adjuvants include, but are not limited to the following:

(i) Acidifying agents, such as, boric acid, acetic acid, glacial acetic acid, citric acid, fumaric acid, hydrochloric acid, diluted hydrochloric acid, malic acid, nitric acid, phosphoric acid, diluted phosphoric acid, sulfuric acid and tartaric acid.

(ii) Alcohol denaturants, such as, denatonium benzoate, methyl isobutyl ketone and sucrose octacetate.

(iii) Alkalizing agents including ammonia solution, ammonium carbonate, diethanolamine, diisopropanolamine, potassium hydroxide, sodium bicarbonate, sodium borate, sodium carbonate, sodium hydroxide or trolamine.

(iv) Antimicrobial preservatives, such as, benzalkonium chloride, benzalkonium chloride solution, benzelthonium chloride, benzoic acid, benzyl alcohol, butylparaben, acetylpyridinium chloride, chlorobutanol, chlorocresol, cresol, dehydroacetic acid, ethylparaben, methylparaben, methylparaben sodium, phenol, phenylethyl alcohol, phenylmercuric acetate, phenylmercuric nitrate, potassium benzoate, potassium sorbate, propylparaben, propylparaben sodium, sodium benzoate, sodium dehydroacetate, sodium propionate, sorbic acid, thimerosal and thymol.

(v) Antioxidants, such as, ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorous acid, monothioglycerol, propyl gallate, sodium formaldehyde sulfoxylate, sodium metabisulfite, sodium thiosulfate, sulfur dioxide, alpha tocopherol and other tocopherols and tocopherol derivatives.

(vi) Buffering Agents, including acetic acid, ammonium carbonate, ammonium phosphate, boric acid, citric acid, lactic acid, phosphoric acid, potassium citrate, potassium metaphosphate, potassium phosphate monobasic, sodium acetate, sodium citrate, sodium lactate solution, dibasic sodium phosphate and monobasic sodium phosphate.

(vii) Ointment Bases, including lanolin, anhydrous lanolin, hydrophilic ointment, white ointment, yellow ointment, polyethylene glycol ointment, petrolatum, hydrophilic petrolatum, white petrolatum, rose water ointment and squalane.

(viii) Plasticizers, e.g. castor oil, diacetylated monoglycerides, diethyl phthalate, glycerin, mono- and di-acetylated monoglycerides, polyethylene glycol, propylene glycol, triacetin and triethyl citrate.

(ix) Solvents, for example, acetone, alcohol, diluted alcohol, amylene hydrate, benzyl benzoate, butyl alcohol, carbon tetrachloride, chloroform, corn oil, cottonseed oil, ethyl acetate, glycerin, hexylene glycol, isopropyl alcohol, methyl alcohol, methylene chloride, methyl isobutyl ketone, mineral oil, peanut oil, polyethylene glycol, propylene carbonate, propylene glycol, sesame oil, water for injection, sterile water for injection, sterile water for irrigation and purified water.

(x) Sorbents, such as, powdered cellulose, charcoal, purified siliceous earth or carbon dioxide sorbents (e.g. barium hydroxide lime, soda lime).

(xi) Stiffening Agents, for example, hydrogenated castor oil, cetostearyl alcohol, cetyl alcohol, cetyl esters wax, hard fat, paraffin, polyethylene excipient, stearyl alcohol, emulsifying wax, white wax and yellow wax.

(xii) Suspending and/or Viscosity-increasing agents and adjuvants for topical gel base including, acacia, agar, alginic acid, aluminum monostearate, bentonite, purified bentonite, magma bentonite, carbomer 940 or 980, carboxymethylcellulose calcium, carboxymethylcellulose sodium, carboxymethycellulose sodium 12, carrageenan, microcrystalline and carboxymethylcellulose sodium cellulose, dextrin, gelatin, guar gum, hydroxyethyl cellulose, hydroxypropyl cellulose, polyoxyethylene-polyoxypropylene-block polymers, hydroxypropyl methylcellulose, magnesium aluminum silicate, methylcellulose, pectin, polyethylene oxide, polyethylene glycol, wood wax, alcohols, polyvinyl alcohol, povidone, propylene

glycol alginate, silicon dioxide, colloidal silicon dioxide, sodium alginate, tragacanth and xanthan gum, cocoa butter, hard fat and polyethylene glycol.

(xiv) Agents that promote penetration, including urea, non-ionic detergents e.g. NP-40, Triton X-100, ionic detergents such as sodium dodecyl sulphate, lauryl decyl sulphate and chaotrophic salts.

The pharmaceutical compositions of the present invention, as well as medicaments prepared by using these compositions may be altered into the form of foam by any method known in the art for producing foam. For detailed description of such methods see: U.S. Patent application 20040057922; U.S. Patent application 20030039614; U.S. Patent application 20020018812; U.S. Pat. No. 6,730,288, all incorporated herein by reference.

The pharmaceutical compositions provided by the present invention, may be administered to the ear of the treated subject through a device in which the compositions would be packed under pressure, prepared to be applied to the treated object in a form of foam, through an extension or tube, said extension adjusted to access the ear in an easy and user friendly manner.

In one embodiment, the foam is ejected through an actuator that is elongated a few centimeters with a narrow stem-like part which ends in a rounded and wider orifice which prevents injury of the ear canal. In light of the wider and rounded tip of the stem, it is difficult, if not impossible to insert it deep into the ear canal. When the foam is ejected into the ear canal it expands and fills the whole ear canal, therefore it contacts with the whole ear canal area. This has many advantages since it enables contact of the active compound (pharmaceutical) for extended periods of time with the walls of the ear canal and therefore exerts its effect.

In one another embodiment, the device is aerosol device. As used herein, the term "aerosol" is directed to a container that contains a liquid with gas under pressure for dispensing said liquid as foam. The use of aerosol device is well known in the art to produce foam. In a nut shell, the aerosol device is composed of standard aerosol cans (such as aluminium or tinplate) which can contain pressure higher than the atmospheric pressure. In the aerosol there is usually a liquid in mono-phasic solution

(i.e. homogeneous solution) or in bi-phasic solution (i.e. aqueous solution and oil solution). The container is tightly closed with a valve orifice. Thereafter a propellant (i.e. a liquefied gas) such as butane, propane or any other propellant as is known in the art is inserted, which creates the pressure inside the container. The way in which a product is dispensed as foam (mousse or gel) is directly influenced by the mixture of the product solution, propellant type and the technical design of the aerosol valve and actuator. Inside the container there is high pressure, (e.g. 3 atmospheres), and when the container is shaken, even minimally, the gas and liquid or liquids are mixed.

Further description of aerosol devices and the creation of foam and dispersion processes are disclosed by way of example in U.S. Pat. No. 5,322,683; US Patent No. 5,397,564; and U.S. Pat. No. 6,730,288 all of which incorporated herein by reference. Non-aerosol foams are also well-known in the art as disclosed by way of example in US Patent Nos. 6,612,468; US Patent No. 6,660,282; and US Patent No. 6,030,931 all of which incorporated herein by reference.

It is explicitly understood that the pharmaceutical composition and methods of the present invention are suitable for pharmacologically active agents whether water soluble, poorly water soluble or water insoluble. The judicious choice of ingredients will allow the use of a foam delivery whether or not active ingredients are water soluble or not. Combinations of active ingredients that are water soluble or insoluble may also be practiced according to the present invention. There are many solutions to the problem of formulation of poorly soluble ingredients for improved drug bioavailability including the use of surfactants, micelle solutions, emulsions, microemulsions and organic cosolvents, as are well known in the art of pharmaceutical formulations.

In one embodiment of the invention, the pharmaceutical composition of the present invention is administered to the treated subject in a metered dose manner. The aerosol formulation is preferably arranged so that each metered dose or "puff" of aerosol will ejaculate a pre-determined volume of foam that would fill the ear canal. The advantage of the metered dose method is that the foam will not spill or reach beyond the ear canal, and a precise amount of the medicament is inserted.

In a preferred embodiment, an amount of 0.1-2.0 cc of aerosol formulation is ejaculated per actuation. More preferably, an amount of 0.2-1 cc of aerosol formulation is ejaculated per actuation of the device. The ejaculated amount is determined according to the age of the treated subject, which affects the volume of the ear canal. For example, the ear canal volume of a newborn in the age of one month is usually around 0.2 cc, of a baby in the age of six months is usually 0.5 cc and around 2.0 cc of children older than twenty four months.

The use of metered dose devices for different applications is well know in the art, and is described in details in U.S. Pat. No. 6,032,836; U.S. Pat. No. 5,697,532; U.S. Pat. No. 5,502,076; U.S. Pat. No. 6,702,155; U.S Pat. Application 20030178022, all incorporated herein by reference.

In a different embodiment, the delivery device of the foam-based formulation of the invention may comprise two parts: one part serves as a container that stores the medicament formulation, and upon pressure the medicament is ejected into the ear, in a metered dose manner in the form of foam. The second part is an extension or tube that leads the foam toward the ear canal.

The subject, treated by the method of the present invention may be a mammalian. In a preferred embodiment, the treated subject is a human being. The method provided is applicable to any age and can be used to newborns as well as adults. In a different embodiment the treated subject is an animal, preferably a domestic mammal, including but not limited to household pets.

It is within the scope of the present invention, to use a pharmaceutical composition in the form of a foam for the treatment of any ear disorder which requires administration of pharmaceutical composition through the external auditory meatus of a treated subject, so as to thereby treat the subject. The ear disorder may include any of the abovementioned disorders. The pharmaceutical composition according to the provided use may include any therapeutically active agent or any other agent disclosed above including antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent or a mixture thereof.

The present invention is further directed to a pharmaceutical composition used for the treatment of ear disorder in a form of foam comprising as an active ingredient one or

more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent or a mixture thereof, together with a pharmaceutically acceptable carrier. In one embodiment, the pharmaceutical composition comprises a medicament.

The present invention also provides a process of preparing a pharmaceutical for the treatment of an ear disorder in a form of foam to thereby treat a subject in need of such treatment comprising:

a. obtaining a pharmaceutical composition known to affect ear disorder; and

b. admixing the pharmaceutical composition of step (a) together with a pharmaceutically acceptable carrier and a solution or a homogeneous dispersion agent.

As used herein the term "dispersion agent" is defined as any reactive particulate used in a dispersion process.

The present invention further provides a method for treatment ear disorder in a subject in need of such treatment comprising:

a. obtaining a pharmaceutical composition known to effect ear disorder; and

b. admixing the pharmaceutical composition of step (a) together with a pharmaceutically acceptable carrier and with a lipid surfactant or a solution or a homogeneous dispersion agent;

c. restoring the mixture formulation of step (b) in a container that enables the dispersion of said mixture in a form of foam; and

d. administering the formulation of step (c) to the external auditory meatus of said subject in a metered dose manner, so as to thereby treat the subject.

In one embodiment of the invention, the pharmaceutical composition used for the treatment of ear disorder in the form of foam may comprise as an active ingredient

one or more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent or a mixture thereof, together with a pharmaceutically acceptable carrier. The treated disorder by the disclosed method may be any of the abovementioned disorders.

In one another embodiment, the lipid surfactant and the dispersion agent used the disclosed methods are being selected from the group consisting of cholesteryl esters, phospholipids, carbohydrates, and proteins, all in powder form. Each metered dose formulation contains an acceptable therapeutic dosage and ejaculates to a final volume which is suitable to fill the ear canal of the treated subject. In a further embodiment, the pharmaceutical composition is used to manufacture a medicament.

The following is a non-limiting description of diseases and disorders that may be amenable to treatment with the compositions and methods of the invention.

External Ear Disorders

Disorders of the outer ear include blockages, infections (external otitis and perichondritis), eczema, and tumors. The outer ear is also prone to certain types of injury. The Merck Manual, Second Home Edition, Chapter 219-220 .Biology of the Ears, Nose, and Throat.

Blockages

Earwax (cerumen) may block the ear canal. Even large amounts of wax often produce no symptoms. Symptoms can range from itching to a loss of hearing. Other blockages can occur when people, particularly children, put foreign objects, such as beads, erasers, and beans, into the ear canal. Insects, particularly cockroaches, may also block the ear canal.

External otitis

External otitis is infection of the ear canal. It may affect the entire canal, as in generalized external otitis, or just one small area, as in a boil (furuncle) or pimple. A variety of bacteria or, rarely, fungi can cause generalized external otitis. Certain people, including those who have allergies, psoriasis, eczema, or scalp dermatitis, are

particularly prone to external otitis. Injuring the ear canal while cleaning it or getting water or irritants such as hair spray or hair dye in the canal often leads to external otitis. External otitis is particularly common after swimming in fresh water pools, in which case it is sometimes called "swimmer's ear". Earplugs and hearing aids make external otitis more likely, particularly if these devices are not properly cleaned.

Acute otitis externa (AOE), affects four in every thousand Americans annually (Hannley MT, Denneny JC, Holzer SS. Use of ototopical antibiotics in treating 3 common ear diseases. *Otolaryngol Head Neck Surg* 2000; 116:934-940), and is reported to be one of the leading causes of physician visits due to ear pain (LaRosa S. Primary Care Management of otitis externa. *Nurse Pract* 1998; 23:125-133).

Some risk factors associated with AOE include living in tropical or humid climates, summer season and swimmers or those who enjoy other water sports (Pelton SI, Klein JO. The draining ear. Otitis media and otitis externa. *Infect Dis Clin North Am* 1988;2: 117-129; Biedlingmaier JF. Two ear problems you may not need to refer. *Postgrad Med* 1994; 96: 141-148). The warm and wet environment in the ear canal makes it an ideal location for bacteria to inhabit and proliferate. Additional risk factors as mentioned above, include insertion of foreign objects into the ear canal, accumulation of cerumen (earwax), hearing aids, and some skin conditions (seborrhea, psoriasis, or eczema) (Biedlingmaier JF. 1994). Foreign objects such as cotton-tipped swabs or anything used to clean the ear may damage and scratch the ear canal, making the area susceptible to infection. The buildup of earwax and the use of hearing aids may also decrease ventilation in the ear and keep the ear canal moist, thus leading to increased chances for developing AOE. Preventive measures to avoid the risk of AOE include keeping the ear canal clean and dry, using earplugs while swimming, avoiding cleaning or scratching ears with cotton-tipped swabs and avoiding shower heads with powerful streams of water directed to the ear canal (LaRosa S. Primary Care Management of otitis externa. *Nurse Pract* 1998; 23:125-133).

Current management of AOE includes cleaning the ear canal and administering topical drops (ear drops). Topical treatments have the advantage of avoiding systemic side effects, enhancing patient compliance, and maximizing treatment outcomes.

Symptoms of generalized external otitis are itching and pain. Sometimes an unpleasant-smelling white or yellow discharge drains from the ear. The ear canal may have no swelling, slight swelling, or in severe cases be swollen completely closed. If the ear canal swells or fills with pus and debris, hearing is impaired. Usually, the canal is tender and hurts if the external ear (pinna) is pulled or if pressure is placed on the fold of skin in front of the ear canal. To a doctor looking into the ear canal through an otoscope (a device for viewing the canal and eardrum), the skin of the canal appears red and swollen and may be littered with pus and debris.

Perichondritis

Perichondritis is infection of the cartilage of the external ear. Injury, burns, insect bites, ear piercing, or a boil on the ear may cause perichondritis. The infection also tends to occur in people whose immune system is weakened and in people who have diabetes. The first symptoms are redness, pain, and swelling of the ear. The person may have a fever. Pus accumulates between the cartilage and the layer of connective tissue around it (perichondrium). Sometimes the pus cuts off the blood supply to the cartilage, destroying it and leading eventually to a deformed ear. Although destructive and long-lasting, perichondritis tends to produce only mild discomfort.

Tumors

Tumors of the ear may be noncancerous (benign) or cancerous (malignant). Noncancerous tumors may develop in the ear canal, blocking it and causing hearing loss and a buildup of earwax. Such tumors include small sacs filled with skin secretions (sebaceous cysts), osteomas (bone tumors), and growths of excess scar tissue after an injury (keloids). Basal cell and squamous cell cancers are common skin cancers that often develop on the external ear after repeated and prolonged exposure to the sun. Ceruminoma (cancer of the cells that produce earwax) develops in the outer third of the ear canal and can spread.

Injury

A number of different injuries can affect the outer ear. A blunt blow to the external ear can cause bruising between the cartilage and the layer of connective tissue around

it (perichondrium). When blood collects in this area, the external ear becomes swollen and purple. The collected blood (hematoma) can cut off the blood supply to the cartilage, allowing that portion of the cartilage to die, leading in time to a deformed ear. This deformity, called a cauliflower ear, is common among wrestlers, boxers, and rugby players. A forceful blow to the jaw may fracture the bones surrounding the ear canal and distort the canal's shape, often narrowing it.

Middle and Inner Ear Disorders

Middle and inner ear disorders produce many of the same symptoms, and a disorder of the middle ear may affect the inner ear and vice versa.

Acute otitis media

Acute otitis media is a bacterial or viral infection of the middle ear. Acute otitis media results from infection by viruses or bacteria, often as a complication of the common cold or of allergies. Acute otitis media is more common in children than in adults. The infected ear is painful, with a red, bulging eardrum. It is usually treated by antibiotics, such as amoxicillin. Acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) can relieve pain. Decongestants containing phenylephrine may help, and antihistamines are useful used for people who have allergies.

Occasionally acute otitis media is complicated with purulent discharge typically via ventilation tubes (in the ear drum) or via perforation in the ear drum, this condition is named suppurative otitis media which can be acute or chronic. Suppurative otitis media is treated mainly with antibiotic ear drops.

Serous otitis media

Serous (secretory) otitis media is an accumulation of fluid in the middle ear. It can develop from acute otitis media that has not completely cleared or from a blocked eustachian tube. Allergies are a common cause of eustachian tube blockage. Serous otitis media can occur at any age but is particularly common in children.

Chronic otitis

Chronic otitis media is a long-standing infection of the middle ear. It is caused by a permanent hole (perforation) in the eardrum or a noncancerous growth of white skin like material (cholesteatoma). People may have a perforation without ever getting any symptoms, but sometimes a chronic bacterial infection develops. Chronic otitis media may flare up after an infection of the nose and throat, such as the common cold, or after water enters the middle ear while bathing or swimming. Usually, flare-ups result in a painless discharge of pus, which may be malodorous, from the ear. Persistent flare-ups may result in the formation of protruding growths called polyps, which extend from the middle ear through the perforation and into the ear canal. Persistent infection can destroy parts of the ossicles, the small bones in the middle ear that connect the eardrum to the inner ear and conduct sounds from the outer ear to the inner ear, causing conductive hearing loss. Other serious complications include inflammation of the inner ear, facial paralysis, and brain infections. Some people with chronic otitis media develop cholesteatomas in the middle ear. Cholesteatomas, which destroy bone, greatly increase the likelihood of other serious complications.

Mastoiditis

Mastoiditis is a bacterial infection in the mastoid process, the prominent bone behind the ear. This disorder usually occurs when untreated or inadequately treated acute otitis media spreads from the middle ear into the surrounding bone, the mastoid process.

Perforation of the Eardrum

A perforation is a hole in the eardrum. A middle ear infection (otitis media) is the most common cause of eardrum perforation. The eardrum can also be perforated by a sudden change in pressure, either an increase, such as that caused by an explosion, a slap, or diving underwater, or a decrease, such as occurs while flying in an airplane. Another cause is burns from heat or chemicals. The eardrum may also be perforated (punctured) by objects placed in the ear, such as a cotton-tipped swab, or by objects entering the ear accidentally, such as a low-hanging twig or a thrown pencil. An object that penetrates the eardrum can dislocate or fracture the chain of small bones (ossicles) that connect the eardrum to the inner ear. Pieces of the broken ossicles or the object itself may even penetrate the inner ear. A blocked eustachian tube may lead

to the perforation because of severe imbalance of pressure (barotrauma). Perforation of the eardrum causes sudden severe pain, sometimes followed by bleeding from the ear, hearing loss, and noise in the ear (tinnitus).

Myringitis

Myringitis is infection of the eardrum caused by a variety of viruses and bacteria; the bacterium Mycoplasma is a common cause. The eardrum becomes inflamed, and small, fluid-filled blisters (vesicles) form on its surface. Blisters may also be present in otitis media; however, in myringitis, there is no pus or fluid in the middle ear.

Meniere's disease

Meniere's disease is a disorder characterized by recurring attacks of disabling vertigo (a whirling sensation), hearing loss, and tinnitus. Meniere's disease is thought to be caused by an imbalance in the fluid that is normally present in the inner ear. This fluid is continually being secreted and reabsorbed, maintaining a constant amount. Either an increase in production of inner ear fluid or a decrease in its reabsorption results in an imbalance of fluid.

Temporal bone fracture

The temporal bone (the skull bone containing part of the ear canal, the middle ear, and the inner ear) can be fractured by a blow to the head. Temporal bone fractures frequently rupture the eardrum and may also damage the ossicles and the cochlea. Symptoms include facial paralysis on the side of the fracture and profound hearing loss, which may be conductive, sensorineural, or both.

Auditory nerve tumors

An auditory nerve tumor (acoustic neuroma, acoustic neurinoma, vestibular schwannoma, eighth nerve tumor) is a noncancerous (benign) tumor that originates in the cells that wrap around the auditory nerve (Schwann cells).

Barotrauma

Barotrauma is damage to the middle ear caused by unequal air pressure on the two sides of the eardrum.

EXAMPLES

The following non-limiting examples of compositions in accordance with the principles of the invention are provided for illustrative purposes only.

EXAMPLE 1 Analgesic ear foam

		% COMPOSITION (of pressurized liquid)
01	antipyrin (active principle)	5
02	tetracaine (active principle)	0.5
03	Potassium metabisulphite (antioxidant)	0.25
04	Sodium benzoate (antibacterial-antimildew agent)	0.38
05	Polysorbate 20 (foaming surfactant)	4
06	Polyglycol 300 isostearate (foam thickener)	4
07	Purified water	75.87
08	propellant	10

Preparation method:

A) The components 03, 04, and 02 are dissolved in 07 in the stated order in a stainless steel dissolving vessel of suitable capacity fitted with a propeller stirrer and turboemulsifier.

B) 05, 06 and finally 01 are added while stirring, and the turboemulsifier is then operated for 15 minutes.

C) Using a metering pump, the suspension is metered in the volume corresponding to the theoretical weight into aerosol cans while stirring.

D) Each can is immediately sealed by clinching the dispenser valve and is then pressurized by means of the propellant, which is fed in under pressure in a suitable quantity by a pumping device.

EXAMPLE 2 Antibiotic ear foam

	% COMPOSITION (of pressurized liquid)

01 Neomycin 5, Polymyxin B 10,000 units/ml, Dexamethasone 1 (active principles)

02	Xanthan gum (active principle thickener and suspension agent)	0.2
03	Potassium metabisulphite (active principle antioxidant)	0.25
04	EDTA bisodium salt (active principle antioxidant)	0.3
05	Polysorbate 20 (foaming surfactant)	4
06	Polyglycol 300 isostearate (foam thickener)	4
07	Purified water	75.25
08	propellant	6.5

Preparation method:

A) The components 03, 04, and 02 are dissolved in 07 in the stated order in a stainless steel dissolving vessel of suitable capacity fitted with a propeller stirrer and turboemulsifier.

B) 05, 06 and finally 01 are added while stirring, and the turboemulsifier is then operated for 15 minutes.

C) Using a metering pump, the suspension is metered in the volume corresponding to the theoretical weight into aerosol cans while stirring.

D) Each can is immediately sealed by clinching the dispenser valve and is then pressurized by means of the propellant, which is fed in under pressure in a suitable quantity by a pumping device

EXAMPLE 3 Antibiotic ear FOAM 0.3% Ofloxacine

		% COMPOSITION (of pressurized liquid)
01	Ofloxacine (active principle)	0.3
02	Dexamethasone (steroid)	1
03	Polysorbate 20 (foaming surfactant)	4
04	Polyglycol 300 isostearate (foam thickener)	4
05	Propyleneglycol	5
06	Purified water	75.7
07	propellant	10

Preparation method:

A) The components 01 and 02 are dissolved in 06 in the stated order in a stainless steel dissolving vessel of suitable capacity fitted with a propeller stirrer and turboemulsifier.

B) 03, 04, 05 and finally 01 are added while stirring, and the turboemulsifier is then operated for 15 minutes.

C) Using a metering pump, the suspension is metered in the volume corresponding to the theoretical weight into aerosol cans while stirring.

D) Each can is immediately sealed by clinching the dispenser valve and is then pressurized by means of the propellant, which is fed in under pressure in a suitable quantity by a pumping device.

EXAMPLE 4 Lipid based mousse formulations.

Lipid based mousse formulations.

	Example 4A	Example 4B	Example 4C	Example 4D
Petrolatum	10-20%	10-20%	10-20%	10-20%
Neomycine	5%			
Polymyxin B	10,000u/ml			
Dexamethasone	1%	1%		1%
Tetracaine			0.5%	
Antipyrine			5%	
ciprofloxacine				0.2%
ofloxacine		0.3%		
Alkyl benzoate	10%	10%	10%	10%
Sorbitan Stearate	2.5-4.5%	2.5-4.5%	2.5-4.5%	2.5-4.5%
Polysorbate 60	2.3-5.7%	2.3-5.7%	2.3-5.7%	2.3-5.7%
Water	20-75%	20-75%	20-75%	20-75%
propellant	5%	5%	5%	5%
Total	100%	100%	100%	100%

It will be appreciated by persons skilled in the art that the present invention is not limited by what has been particularly shown and described herein above. Rather the scope of the invention is defined by the claims that follow. The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without undue

experimentation and without departing from the generic concept, and, therefore, such adaptations and modifications should and are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation. The means, materials, and steps for carrying out various disclosed functions may take a variety of alternative forms without departing from the scope of the invention.

CLAIMS

1. A method for the treatment of ear disorder in a subject in need of such treatment comprising administering an amount of a pharmaceutical composition in a form selected from a foam and a mousse through the external auditory meatus of said subject so as to thereby treat the ear disorder.

2. The method of claim 1, wherein the ear disorder is a condition that requires administration of a pharmaceutical composition into the ear canal of the treated subject, so as to thereby treat the subject.

3. The method of claim 1, wherein the ear disorder is otitis externa.

4. The method of claim 3, wherein the otitis externa is acute otitis externa.

5. The method of claim 1, wherein the ear disorder is acute otitis media.

6. The method of claim 1, wherein the ear disorder is suppurative otitis media.

7. The method of claim 1, wherein the ear disorder is any infection of the inner ear.

8. The method of claim 1, wherein the ear disorder is mastoiditis.

9. The method of claim 1, wherein the ear disorder is ruptured eardrum.

10. The method of claim 1, wherein the ear disorder is otalgia induced by any physical or biological cause.

11. The method of claim 15, wherein the otalgia is caused as a result of an allergic reaction.

12. The method of claim 15, wherein the otalgia is caused as a result of either acute or chronic sinusitis.

13. The method of claim 15, wherein the otalgia is caused as a result of tooth abscess.

14. The method of claim 15, wherein the otalgia is caused as a result of sore throat with referred pain to the ear.

15. The method of claim 1, wherein the pharmaceutical composition comprises one or more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent and a mixture thereof, in a therapeutic effective amount.

16. The method of claim 15, wherein the antibiotic agent is selected from the group consisting of amikacin, gentamycin, tobramycin, streptomycin, netilmycin, kanamycin ciprofloxacin, norfloxacin, ofloxacin, trovafloxacin, lomefloxacin, levofloxacin, enoxacin, sulfonamides, polymyxin, chloramphenicol, neomycin, paramomomycin, colistimethate, bacitracin, vancomycin, tetracyclines, rifampins, cycloserine, beta-lactams, cephalosporins, and pharmaceutically acceptable derivatives thereof.

17. The method of claim 15, wherein the antibacterial agent is either acetic acid or boric acid or a mixture thereof.

18. The method of claim 15, wherein the steroid agent is selected from the group consisting of betamethasone, betamethasone dipropionate, fluocinonide, fluocinoline acetonide, hydrocortisone, methylprednisolone, clobetasol, beclomethasone, dexamethasone sodium phosphate, triamcinolone and pharmaceutically acceptable derivatives thereof.

19. The method of claim 15, wherein the antifungal agent is selected from the group consisting of amphotericins, fluconazole, flucytosine, natamycin, miconazole, ketoconazole, amphotericin B, nystatin, cromolyn, lodoxamide, levocabastin, naphazolin, antazoline, pheniramimane and pharmaceutically acceptable derivatives thereof.

20. The method of claim 15, wherein the antiinflammatory agent is selected from the group consisting of non-steroidal anti-inflammatory agents (NSAID), antipyrin and pharmaceutically acceptable derivatives thereof.

21. The method of claim 15, wherein the local anesthetic agent is selected from the group consisting of benzocaine, benzyl benzoate, bupivacaine, calamine, chloroprocaine, chloroxylenol, cinchocaine, cocaine, dexivacaine, diamocaine, dibucaine, dyclonine, etidocaine, hexylcaine, ketamine, levobupivacaine, lidocaine, menthol, mepivacaine, oxethazaine, phenol, pramoxine, prilocaine, amethocaine, tetracaine, proparacaine, propoxycaine, pyrrocaine, resorcinol, risocaine, rodocaine, ropivacaine, tetracaine, troclosan, and pharmaceutically acceptable derivatives thereof.

22. The method of claim 1, wherein said pharmaceutical composition is administered via a metered dose device.

23. The method of claim 1, wherein the treated subject is a mammal.

24. The method of claim 23, wherein said mammal is a human being.

25. The method of claim 23, wherein said mammal is a domestic animal.

26. Use of a pharmaceutical composition in a form selected from a foam and a mousse for the treatment of any ear disorder which requires administration of a pharmaceutical composition through the external auditory meatus of a treated subject, so as to thereby treat the ear disorder.

27. The use according to claim 26, wherein the ear disorder is any condition that requires administration of any pharmaceutical composition into the ear canal of the treated subject, so as to thereby treat the subject.

28. The use according to claim 26, wherein the ear disorder is selected from the group consisting of otitis externa, acute otitis media, chronic suppurative otitis media, infections of the inner ear, mastoiditis, perforation of the tympanic membrane, ruptured eardrum, otalgia caused by any physical or biological cause including allergic reactions, acute sinusitis, chronic sinusitis, tooth abscess, sore throat with referred pain to the ears, and any other condition that requires administration of any kind of medicament into the ear canal of a treated object.

29. Use of a pharmaceutically active agent to manufacture a medicament in the form selected from a foam and a mousse for the treatment of any ear disorder which requires administration of a pharmaceutical composition through the external auditory meatus of a treated subject, so as to thereby treat the ear disorder.

30. 30. The use according to claim 29, wherein the medicament comprises one or more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent or a mixture thereof in a therapeutically acceptable amount.

31. A pharmaceutical composition for the treatment of ear disorder in a form selected from a foam or a mousse comprising as an active ingredient one or more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent or a mixture thereof, together with a pharmaceutically acceptable carrier.

32. A process of preparing a medicament for the treatment of ear disorder in the form of a foam comprising:

a. providing a pharmaceutical agent known to affect an ear disorder;

b. admixing the pharmaceutical agent of step (a) with a suitable pharmaceutically acceptable carrier comprising a homogeneous dispersion agent;

c. providing a propellant.

33. A method for treatment ear disorder in a subject in need of such treatment comprising:

a. providing a pharmaceutical agent known to affect an ear disorder;

b. admixing the pharmaceutical agent of step (a) together with a pharmaceutically acceptable carrier comprising a lipid surfactant and homogeneous dispersion agent;

c. storing the mixture formulation of step (b) in a container that enables the dispersion of said mixture in a form selected from a foam or mousse; and

d. administering the formulation of step (c) to the external auditory meatus of said subject in a metered dose manner, so as to thereby treat the ear disorder.

34. The method of claim 33, wherein said lipid surfactant and said dispersion agent of step (b) are being selected from the group consisting of cholesteryl esters, phospholipids, carbohydrates, and proteins, all in powder form.

35. The method of claim 33, wherein each metered dose of the formulation provides an acceptable therapeutic dosage in a final volume which is suitable to fill the ear canal of the treated subject

36. The method of claim 33, wherein the ear disorder is any condition that requires administration of any pharmaceutical composition into the ear canal of the treated subject, so as to thereby treat the ear disorder.

37. The method of claim 33, wherein the pharmaceutical composition comprises one or more antibiotic agent, antibacterial agent, antifungal agent, steroid agent, anti-inflammatory agent, local anesthetic agent and a mixture thereof, in a therapeutically effective amount.

38. The method of claim 37, wherein the antibiotic agent is selected from the group consisting of amikacin, gentamycin, tobramycin, streptomycin, netilmycin, kanamycin ciprofloxacin, norfloxacin, ofloxacin, trovafloxacin, lomefloxacin, levofloxacin, enoxacin, sulfonamides, polymyxin, chloramphenicol, neomycin, paramomomycin, colistimethate, bacitracin, vancomycin, tetracyclines, rifampins, cycloserine, beta-lactams, cephalosporins, and pharmaceutically acceptable derivatives thereof.

39. The method of claim 37, wherein the antibacterial agent is either acetic acid or boric acid or a mixture thereof.

40. The method of claim 37, wherein the steroid agent is selected from the group consisting of betamethasone, betamethasone dipropionate, fluocinonide, fluocinoline acetonide, hydrocortisone, methylprednisolone, clobetasol, beclomethasone, dexamethasone sodium phosphate, triamcinolone and pharmaceutically acceptable derivatives thereof.

41. The method of claim 37, wherein the antifungal agent is selected from the group consisting of amphotericins, fluconazole, flucytosine, natamycin, miconazole, ketoconazole, amphotericin B, nystatin, cromolyn, lodoxamide, levocabastin, naphazolin, antazoline, pheniramimane and pharmaceutically acceptable derivatives thereof.

42. The method of claim 37, wherein the antiinflammatory agent is selected from the group consisting of non steroidal anti-inflammatory agents (NSAID), antipyrin and pharmaceutically acceptable derivatives thereof.

43. The method of claim 37, wherein the local anesthetic agent is selected from the group consisting of benzocaine, benzyl benzoate, bupivacaine, calamine, chloroprocaine, chloroxylenol, cinchocaine, cocaine, dexivacaine, diamocaine, dibucaine, dyclonine, etidocaine, hexylcaine, ketamine, levobupivacaine, lidocaine, menthol, mepivacaine, oxethazaine, phenol, pramoxine, prilocaine, amethocaine, tetracaine, proparacaine, propoxycaine, pyrrocaine, resorcinol, risocaine, rodocaine, ropivacaine, tetracaine, troclosan, and pharmaceutically acceptable derivatives thereof.

ABSTRACT

The present invention relates to medicaments used for the treatment of ear disorders, administered to a treated ear in a pharmaceutical composition selected from a foam or mousse. Administering a medicament in such forms will increase the residence time of the medicament in the ear canal, provide relatively uniform distribution of the composition, and can increase the penetration of the active pharmaceutical ingredient in the affected area, may release active substances slowly, enhance treatment effectiveness, increase compliance and could be more convenient to use than currently available ear medications. The adminstration in the form of a foam or a mousse may preferably be provided as a metered dose, of a volume suitable to fill the ear canal.